REMARKS

Claims 111-170 are pending in the present application. Reconsideration and allowance of the present application in view of the following remarks are respectfully requested.

I. THE CLAIM REJECTIONS UNDER 35 U.S.C. § 103(a) SHOULD BE WITHDRAWN

The pending claims have been rejected under 35 U.S.C. § 103 as allegedly being unpatentable over U.S. Patent No. 5,464,650 to Berg *et al.* (hereinafter "Berg") alone, or Berg in further view of U.S. Patent No. 5,288,711 to Mitchell *et al.* (hereinafter "Mitchell"). For the following reasons, Applicants respectfully disagree.

1. The Legal Standard

A finding of obviousness requires that "the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains." 35 U.S.C. § 103(a). In its recent decision addressing the issue of obviousness, *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 82 USPQ2d 1385 (2007), the Supreme Court stated that the following factors set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966) still control an obviousness inquiry: (1) the scope and content of the prior art; (2) the differences between the prior art and the claimed invention; (3) the level of ordinary skill in the art; and (4) objective evidence of nonobviousness. *KSR*, 127 S. Ct. at 1734, 82 USPQ2d at 1388 quoting *Graham*, 383 U.S. at 17-18, 14 USPQ at 467.

The Supreme Court rejected a rigid application of the "teaching, suggestion, or motivation" test previously applied by the Court of Appeals for the Federal Circuit. *KSR*, 127 S. Ct. at 1739, 82 USPQ2d at 1395. However, the Supreme Court affirmed that it is "important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does...because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known." *KSR*, 127 S. Ct. at 1741, 82 USPQ2d at 1396. Thus, consistent with the principles enunciated in *KSR*, a *prima facie* case of obviousness can be established by showing a suggestion or motivation, either in the references themselves or in the knowledge

generally available to one of ordinary skill in the art, to modify the reference *and* to carry out the modification with a reasonable expectation of success, viewed in light of the prior art. Both the suggestion and the reasonable expectation of success must *not* be based on the applicant's disclosure. *In re Dow Chemical Co.*, 837 F.2d 469, 5 USPQ2d 1529 (Fed. Cir. 1988).

With regard to the final point, the Supreme Court in *KSR* citing *Graham*, upheld the principle of *avoiding hindsight bias* and cautioned courts to *guard against reading into the prior art the teachings of the invention in issue*. 127 S. Ct. at 1742, 82 USPQ2d at 1397:

> A factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon *ex post* reasoning. See *Graham*, 383 U.S., at 36, 86 S.Ct. 684 (warning against a "temptation to read into the prior art the teachings of the invention in issue" and instructing courts to "'guard against slipping into the use of hindsight'" (quoting *Monroe Auto Equipment Co. v. Heckethorn Mfg. & Supply Co.*, 332 F.2d 406, 412 (C.A.6 1964))).

Thus, the principles set forth in *Graham* and in *Dow Chemical* – which are still good law post-*KSR* – require that *both* the suggestion and the expectation of success must be found in the prior art, and not from knowledge gained from the applicant's disclosure.

In support of this requirement, the Office's examination guidelines for determining obviousness specify that after resolution of the Graham factual inquiries, the Office personnel must articulate all three of the following findings to explain a conclusion of obviousness:

> (1) a finding that there was some teaching, suggestion, or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings;
> (2) a finding that there was reasonable expectation of success; and
> (3) whatever additional findings based on the Graham factual inquiries may be necessary, in view of the facts of the case under consideration, to explain a conclusion of obviousness.

Notice entitled "Examination Guidelines for Determining Obviousness Under 35 U.S.C. 103 in View of the Supreme Court Decision in *KSR International Co.* v. *Teleflex Inc.*" 72 Fed. Reg. 57526, 57534 (October 10, 2007).

2. The Claims Are Patentable Over Berg

Claims 111-113, 120-121, 124-125, 129-130, 136-137, 139-143, 150-151, 154-155, 159-160, 166-167, and 169-170 are rejected under 35 U.S.C. § 103(a), as allegedly being unpatentable over Berg. Specifically, the Examiner acknowledges that Berg fails to teach that the topcoat is free of an elutable material (see Office Action, page 3, lines 3-4). Nevertheless, the Examiner contends that Berg's disclosure of a therapeutic substance to polymer ratio which could range from about 10:1 to about 1:100 suggests a topcoat which is "substantially free" of an elutable material. According to the Examiner, a person having ordinary skill in the art would therefore expect the topcoat of Berg to have the same properties as the present invention (see Office Action, page 5, ¶2, lines 2-4). For the following reasons, Applicants respectfully disagree.

The Examiner's contention is erroneous in several aspects. First, Berg discloses coating configurations having a higher ratio of drug (which is an elutable material)-to-polymer in the outer layers than in the inner layers of the coating configuration (2:64-68). However, Berg is silent as a stent having the opposite coating configuration, *i.e.*, a stent having a higher drug-to-polymer ratio in the inner layer than in the outer layers.

Also, Berg suggests that a drug, which is an elutable material, is always present in each layer of the coating configuration. All of Berg's working examples, for instance, disclose coating compositions that contain a high drug-to-polymer ratio (*i.e.*, 2-to-1) (see Examples 3-7 on col. 6, line 1, to col. 7, line 15).

Moreover, Berg's mere disclosure of a drug-to-polymer ratio of 1:100 does not disclose or suggest a coating configuration in which a topcoat is substantially free of a therapeutic agent while an undercoat includes a higher drug-to-polymer ratio. In particular, Berg does not teach or suggest that the 1:100 ratio should be used in an outer layer of its coating configuration while an inner layer of the coating configuration has a higher ratio of drug-to-polymer.

Furthermore, Applicants submit that Berg does not teach or suggest a stent having a coating comprising an undercoat and a topcoat each having a different polymer and different concentration of therapeutic substance wherein the topcoat is free of any therapeutic substance, as recited in the claims. The stents in Berg's working examples were all prepared using a uniform coating composition. None of the stents prepared in Berg's working examples have a plurality of layers having a different polymer and/or a different

concentration of therapeutic substance wherein the topcoat is free of any therapeutic substance.

Thus, based on Berg, a person of ordinary skill in the art could not predict a stent having a topcoat "substantially free" of an elutable material, let alone a topcoat free of elutable material. U.S. Patent No. 5,492, 895 to Vlasuk *et al.* (cited for the proposition that hirudin is a smooth muscle cell inhibitor) fails to remedy this deficiency. Here, it appears that the Examiner has impermissibly relied on knowledge gained from Applicants' own disclosure for the teaching or suggestion of a topcoat free of elutable material, and thus has read the teachings of Applicants' disclosure into Berg. Such hindsight bias should be avoided. *KSR*, 127 S. Ct. at 1742, 82 U.S.P.Q.2d at 1397.

Second, the rejection fails to account for the failure of Berg to teach or suggest the particular polymer combinations recited in the undercoat and topcoat of the claimed stents. According to the MPEP, in making an obviousness determination, the number of variables which must be selected or modified must be considered, as well as the nature and significance of the differences between the prior art and the claimed invention. See § MPEP 2144.08, subsection II.A.4(c), at page 2100-148; and *see, e.g., In re Jones*, 958 F.2d 347, 350, 21 U.S.P.Q.2d 1941, 1943 (Fed. Cir. 1992).

In particular, Berg fails to teach or suggest selecting a hydrophobic elastomeric material (*e.g.*, ethylene vinyl acetate) to be included in an undercoat of a stent, as recited in the claims. Instead, Berg indiscriminately identifies both hydrophilic (*e.g.*, polyamino acids, fibrin, starch, carboxymethyl cellulose) and hydrophobic (*e.g.*, polyurethanes, silicones) polymers as being suitable for coating a stent. *See* Berg, col. 4, *l.* 35, to col. 5, *l.* 7. Moreover, Berg is silent as to the desirability of having a hydrophobic material in an undercoat of a multilayered stent. Thus, one skilled in the art, in view of Berg, would not find any suggestion or motivation to select a *hydrophobic* elastomeric material to form the undercoat of the claimed stents.

Berg also fails to teach or suggest selecting a *biostable*, non-thrombogenic polymeric material to be included in the topcoat of a stent, as recited in the claims. In fact, Berg teaches away from including a biostable polymer in the topcoat. Berg states that in choosing between a biostable or bioavailable polymer, "a *bioabsorbable* polymer is probably more desirable since, unlike a biostable polymer, it will not be present long after implantation to cause any adverse, chronic local response." *See* Berg, col. 4, *ll.* 39-42 (emphasis added). In fact, all of Berg's working examples illustrate stents formed from a uniform coating composition

comprising bioabsorbable polymers (*e.g.*, polycaprolactone and polylactic acid polymers). *See* Berg, col. 6, *l.* 1, to col. 7, *l.* 15. Thus, one skilled in the art, in view of Berg, would not find any suggestion or motivation to select a *biostable* polymeric material to form the topcoat of the claimed stents. In addition, Berg never mentions use of a biostable, *non-thrombogenic* polymeric material.

Given the number of variables which must be selected and modified by the skilled artisan, as well as the differences between Berg and the claimed invention, Applicants submit that Berg fails to teach or suggest the claimed stent. For at least the foregoing reasons, Applicants submit that the Examiner has failed to establish a *prima facie* case of obviousness, and thus, submit that the rejection is in error and should be withdrawn.

3. The Claims Are Patentable Over Berg in Further View of Mitchell

Claims 114-119, 122-123, 126-128, 131-135, 138, 144-149, 152-153, 156-158, 161-165 and 168 are rejected under 35 U.S.C. § 103(a), as allegedly being unpatentable over Berg in further view of Mitchell. Specifically, the Examiner acknowledges that Berg fails to disclose a coating comprising an antibiotic, but relies on Mitchell for the disclosure of a stent comprising an antibiotic to inhibit proliferation of vascular smooth muscle cells (Office Action, p. 4, ¶1). The Examiner contends that "[i]t would have been obvious to one of ordinary skill in the art to combine the teaching of a stent comprising an antibiotic as taught by Mitchell et al., to a coated vascular stent as per Berg et al." (Office Action, p. 4, *ll.* 6-9). For the following reasons, Applicants respectfully disagree.

As discussed above, Berg fails to render predictable a stent having a topcoat that is free of an elutable material. Nor does Berg teach or suggest a stent having the particular polymer combination used in an undercoat and a topcoat, much less teach or suggest a stent having the particular polymer combination and drug concentration in an undercoat and a topcoat. Mitchell fails to remedy these deficiencies. In fact, Mitchell never teaches or suggests a polymer coating being disposed on a stent, much less teach or suggest a stent having more than one coating (*i.e.*, an undercoat and a topcoat) having the particular polymer and drug combination recited in the claims. Since the combination of Berg and Mitchell fails to teach or suggest each and every element of the claimed stents, Applicants respectfully submit that the claims are patentable over Berg and Mitchell. Thus, the rejection is in error and should be withdrawn.

CONCLUSION

As all rejections are believed to be overcome, all claims are believed to be in condition for allowance. An early notice to that effect would be appreciated. Should the Examiner not agree with Applicants' position, then a personal or telephonic interview is respectfully requested to discuss any remaining issues and expedite the eventual allowance of the application.

Respectfully submitted,

Date: October 30, 2007

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